MMR Vaccine & Autism
(Measles, Mumps, and Rubella)

At a glance: The weight of currently available scientific evidence does not support the hypothesis that MMR vaccine causes autism. CDC recognizes there is considerable public interest in this issue, and therefore supports additional research regarding this hypothesis. CDC is committed to maintaining the safest, most effective vaccine supply in history.

1. What is autism?

Autism is a term that refers to a collection of neurologically-based developmental disorders in which individuals have impairments in social interaction and communication skills, along with a tendency to have repetitive behaviors or interests. The severity of autism varies greatly, from individuals with little speech and poor daily living skills, to others who function well in most settings. Autism is typically diagnosed during the toddler or preschool years, although some children are diagnosed at older ages. It has been reported that approximately 20 percent of children with autism experience a "regression;" that is, they have apparently normal development followed by a loss of communication and social skills. Boys are three-to-four times more likely to have autism than girls. Autism occurs in all racial, ethnic, and social groups. A variety of factors could be associated with some forms of autism, including infectious, metabolic, genetic, neurological, and environmental factors. Genetic factors and brain abnormalities at birth are considered to be some of the most recognized causes of autism. For more information, see Autism Questions & Answers.

2. Does the measles-mumps-rubella (MMR) vaccine cause autism?

Current scientific evidence does not support the hypothesis that measles-mumps-rubella (MMR) vaccine, or any combination of vaccines, causes the development of autism, including regressive forms of autism. The question about a possible link between MMR vaccine and autism has been extensively reviewed by independent groups of experts in the U.S. including the National Academy of Sciences, Institute of Medicine. These reviews have concluded that the available epidemiologic evidence does not support a causal link between MMR vaccine and autism.

3. What have studies found regarding MMR vaccine and autism?

Epidemiologic studies have shown no relationship between MMR vaccination in children and development of autism:

- In 1997, the National Childhood Encephalopathy Study (NCES) was examined to see if there was any link between measles vaccine and neurological events. The

researchers found no indication that measles vaccine contributes to the development of long-term neurological damage, including educational and behavioral deficits (Miller et al., 1997).

- A study by Gillberg and Heijbel (1998) examined the prevalence of autism in children born in Sweden from 1975-1984. There was no difference in the prevalence of autism among children born before the introduction of the MMR vaccine in Sweden and those born after the vaccine was introduced.
- In 1999, the British Committee on Safety of Medicines convened a "Working Party on MMR Vaccine" to conduct a systematic review of reports of autism, gastrointestinal disease, and similar disorders after receipt of MMR or measles/rubella vaccine. It was concluded that the available information did not support the posited associations between MMR and autism and other disorders.
- Taylor and colleagues (1999) studied 498 children with autism in the UK and found the age at which they were diagnosed was the same regardless of whether they received the MMR vaccine before or after 18 months of age or whether they were never vaccinated. Importantly, the first signs or diagnoses of autism were not more likely to occur within time periods following MMR vaccination than during other time periods. Also, there was no sudden increase in cases of autism after the introduction of MMR vaccine in the UK. Such a jump would have been expected if MMR vaccine was causing a substantial increase in autism.
- Kaye and colleagues (2001) assessed the relationship between the risk of autism among children in the UK and MMR vaccine. Among a subgroup of boys aged 2-5 years, the risk of autism increased almost 4 fold from 1988 to 1993, while MMR vaccination coverage remained constant at approximately 95% over these same years.
- Researchers in the U.S. found that among children born between 1980 and 1994 and enrolled in California kindergartens, there was a 373% relative increase in autism cases, though the relative increase in MMR vaccine coverage by the age of 24 months was only 14% (Dales et al., 2001). For more on this study, see California Data on Theory of Autism and MMR Immunization.
- Researchers in the UK (Frombonne & Chakrabarti, 2001) conducted a study to test the idea that a new form, or "new variant," of Inflammatory Bowel Disease (IBD) exists. This new variant IBD has been described as a combination of developmental regression and gastrointestinal symptoms occurring shortly after MMR immunization. Information on 96 children (95 immunized with MMR) who were born between 1992 and 1995 and were diagnosed with pervasive developmental disorder were compared with data from 2 groups of autistic patients (one group of 98 born before MMR was ever used and one group of 68 who were likely to have received MMR vaccine). No evidence was found to support a new syndrome of MMR-induced IBD/autism. For instance, the researchers found that there were no differences between vaccinated and unvaccinated groups with regard to when their parents first became concerned about their child's development. Similarly, the rate of developmental regression reported in the vaccinated and unvaccinated groups was not different; therefore, there was no suggestion that developmental regression had increased in frequency since MMR was introduced. Of the 96 children in the first group, no

inflammatory bowel disorder was reported. Furthermore, there was no association found between developmental regression and gastrointestinal symptoms.

- Another group of researchers in the UK (Taylor et al., 2002) also examined whether MMR vaccination is associated with bowel problems and developmental regression in children with autism, looking for evidence of a "new variant" form of IBD/autism. The study included 278 cases of children with autism and 195 with atypical autism (cases with many of the features of childhood autism but not quite meeting the required criteria for that diagnosis, or with atypical features such as onset of symptoms after the age of 3 years). The cases included in this study were born between 1979 and 1998. The proportion of children with developmental regression or bowel symptoms did not change significantly from 1979 to 1988, a period which included the introduction of MMR vaccination in the UK in 1988. No significant difference was found in rates of bowel problems or regression in children who received the MMR vaccine before their parents became concerned about their development, compared with those who received it only after such concern and those who had not received the MMR vaccine. The findings provide no support for an MMR associated "new variant" form of autism and further evidence against involvement of MMR vaccine in autism.

4. Are there studies that suggest there might be a connection between autism and MMR vaccine?

The existing studies that suggest a causal relationship between MMR vaccine and autism have generated media attention. However, these studies have significant weaknesses and are far outweighed by the epidemiologic studies described above that have consistently failed to show a causal relationship between MMR vaccine and autism.

- The MMR-autism theory is based on the idea that intestinal problems, like Crohn's disease, are the result of viral infection and can contribute to the development of autism. The theory has its origins in research by Wakefield and colleagues (1989; 1990) which suggested that inflammatory bowel disease (IBD) is linked to persistent viral infection.
- In 1993, Wakefield and colleagues reported isolating measles virus in the intestinal tissue of persons with IBD. However, the validity of this finding was later called into question when it could not be reproduced by other researchers (Afzal, 1998; Iizuka et al., 2000).
- Thompson and colleagues (1995) suggested in a retrospective cohort study that MMR vaccine might be a risk factor for Crohn's disease. However, the selection and recall biases and the differences in data collection in this study were so substantial as to cast doubt on the validity of the findings.
- Two studies out of Sweden linked measles infection in utero to the development of IBD (Ekbom et al., 1994; Ekbom et al., 1996). However, these studies involved a very small number of cases and when researchers identified the persons to be included in the 1996 study, they had prior knowledge that cases of Crohn's disease had occurred in the offspring of two women who were infected with

measles during pregnancy. This is called "selection bias" and limits the strength of the study.

- The MMR-autism theory came to the forefront when, in 1998, Wakefield and colleagues reviewed reports of children with bowel disease and regressive developmental disorders, mostly autism. The researchers suggested that MMR vaccination led to intestinal abnormalities, resulting in impaired intestinal function and developmental regression within 24 hours to a few weeks of vaccination. This hypothesis was based on 12 children. In 9 of the cases, the child's parents or pediatrician speculated that the MMR vaccine had contributed to the behavioral problems of the children in the study. There are a number of limitations in the Wakefield et al. (1998) study:

1. The study used too few cases to make any generalizations about the causes of autism; only 12 children were included in the study. Further, the cases were referred to the researchers and may not be a representative sample of cases of autism.
2. There were no healthy control children for comparison. As a result, it is difficult to determine whether the bowel changes seen in the 12 children included in the study were similar to changes in normal children, or to determine if the rate of vaccination in autistic children was higher than in the general population.
3. The study did not identify the time period during which the cases were identified.
4. In at least 4 of the 12 cases, behavioral problems appeared before the onset of symptoms of bowel disease; that is, the effect preceded the proposed cause. It is unlikely, therefore, that bowel disease or the MMR vaccine triggered the autism.

- In another study that generated media attention and raised public concern in the UK (Uhlmann et al, 2002), researchers found measles virus fragments in the intestines of children with "new variant" IBD (children with both IBD and developmental disorder). Scientists looked for the presence of measles virus in the intestinal tissue of 91 children with new variant IBD and 70 "controls" (children without this type of IBD). The researchers found measles virus fragments in 75 out of the 91 children with "new variant" IBD, and in only 5 of the 70 controls. While this provides evidence for an association between the presence of measles virus and IBD in children with developmental disorder, it does not mean that the measles component of the MMR vaccine causes IBD or developmental disorder. As a commentary published with the article asserts, the data could just as easily be interpreted as indicating that the IBD or the developmental disorder cause the persistence of measles in the intestines (Morris & Aldulaimi, 2002). In addition, the researchers did not compare the virus found in the intestines of patients with the virus used in the MMR vaccine; nor did they provide information regarding whether or not the children in the study had been previously vaccinated with MMR or had previously contracted measles disease. The limitations of this study are further discussed in a letter written by the Director of CDC's National Immunization Program to the UK's Chief Medical Officer.

5. What about the claim that the number of children with autism has been increasing ever since the MMR vaccine has been in use?

Data from California (Department. of Developmental Services, 1999) have been used to illustrate an increase in cases of autism since the introduction of MMR vaccine. However, the data have been presented inaccurately (Fombonne, 2001). Fombonne (2001) lists several reasons why the data are misrepresented, for instance:

1. the figures presented are based on numbers, not rates and do not account for population growth and changes in the composition of the population,
2. changes in diagnostic definitions were not controlled in the report, and
3. as in other areas of the country, children with autism are currently being diagnosed at earlier ages meaning that there will be an increase in the number of reported cases.

A 2001 study (Dales et al.) used the autism case numbers provided by the California Department of Developmental Services and compared them with early childhood MMR immunization level estimates for California children. Results showed that for children born from 1980 through 1987, there was no major change in MMR immunization levels with the exception of a small increase in children born in 1988. This small increase was followed again by steady levels in children born through 1994. On the other hand, the cases of autism increased markedly, from 44 cases per 100,000 live births in 1980 to 208 cases per 100,000 live births in 1994. Even if one allows that a true increase in autism has occurred and the increase is not due to changes in diagnostic methods, diagnostic categorization, and improved identification of individuals with autism because of the level of services offered (Fombonne, 2001), this analysis shows that receipt of the MMR vaccine is not a factor. If it were a factor, one would expect the shape of the MMR level of immunization curve to be very similar to the autism case numbers. This is not the case, thus the analysis in this study argues against a link between MMR vaccination and autism.

6. Would it be safer to separate the MMR vaccine into its individual components--in other words, give children three separate shots, at different times (e.g., six months or one year apart), instead of one combined shot?

There is no confirmed scientific research or data to indicate that there is any benefit to separating the MMR vaccine into its individual components. A publication by Wakefield and Montgomery (2001) suggests that there is an increased risk of immune-mediated disease when the MMR vaccine is administered as one vaccine versus when the 3 vaccines are administered separately. The specific issue of the safety of multiple vaccines given as one vaccine was addressed by the Institute of Medicine (IOM) (1994, p.63). They stated that the number of separate antigens in a vaccine would not likely result in a significant burden on the immune system that would result in immunosuppression. The issue of multiple vaccines and immune dysfunction was addressed again by the IOM in 2002. An IOM Immunization Safety Review Committee concluded that a review of the available scientific evidence does not support the suggestion that the infant immune

system is inherently incapable of handling the number of antigens that children are exposed to during routine immunizations. The IOM committee also did not suggest any need to change the current US vaccination schedule for MMR.

Splitting the MMR vaccine into three separate doses given at three different times would cause more discomfort from additional injections and would leave children exposed to potentially serious diseases. For instance, if rubella vaccine were delayed, 4 million children would be susceptible to rubella for an additional 6 to 12 months. This would potentially allow otherwise preventable cases of congenital rubella syndrome (CRS) to occur through transmission of rubella from infected children to pregnant women. Ironically, infection of pregnant woman with "wild" rubella virus is one of the few known causes of autism. Thus, by preventing rubella infection of pregnant women, MMR vaccine also prevents autism.

7. Should a younger sibling of an autistic child, or a child of someone who has autism be vaccinated with MMR or other vaccines?

Yes. Current scientific evidence does not show that MMR vaccine, or any combination of vaccines, causes the development of autism, including regressive forms of autism.

A younger sibling or the child of someone who suffered a vaccine side effect usually can, and should, safely receive the same vaccine. This is especially true since the large majority of side effects after vaccination are local reactions and fever, which do not represent a contraindication.

8. Should we delay vaccination until we know more about the negative effects of vaccines?

No. There is no convincing evidence that vaccines such as MMR cause long term health effects. On the other hand, we do know that people will become ill and some will die from the diseases this vaccine prevents. Measles outbreaks have recently occurred in the UK and Germany following an increase in the number of parents who chose not to have their children vaccinated with the MMR vaccine. Discontinuing a vaccine program based on unproven theories would not be in anyone's best interest. Isolated reports about these vaccines causing long term health problems may sound alarming at first. However, careful review of the science reveals that these reports are isolated and not confirmed by scientifically sound research. Detailed medical reviews of health effects reported after receipt of vaccines have often proven to be unrelated to vaccines, but rather have been related to other health factors. Because these vaccines are recommended widely to protect the health of the public, research on any serious hypotheses about their safety are important to pursue. Several studies are underway to investigate still unproven theories about vaccinations and severe side effects.